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Study suggests foods like licorice can be used to 'landscape' your gut

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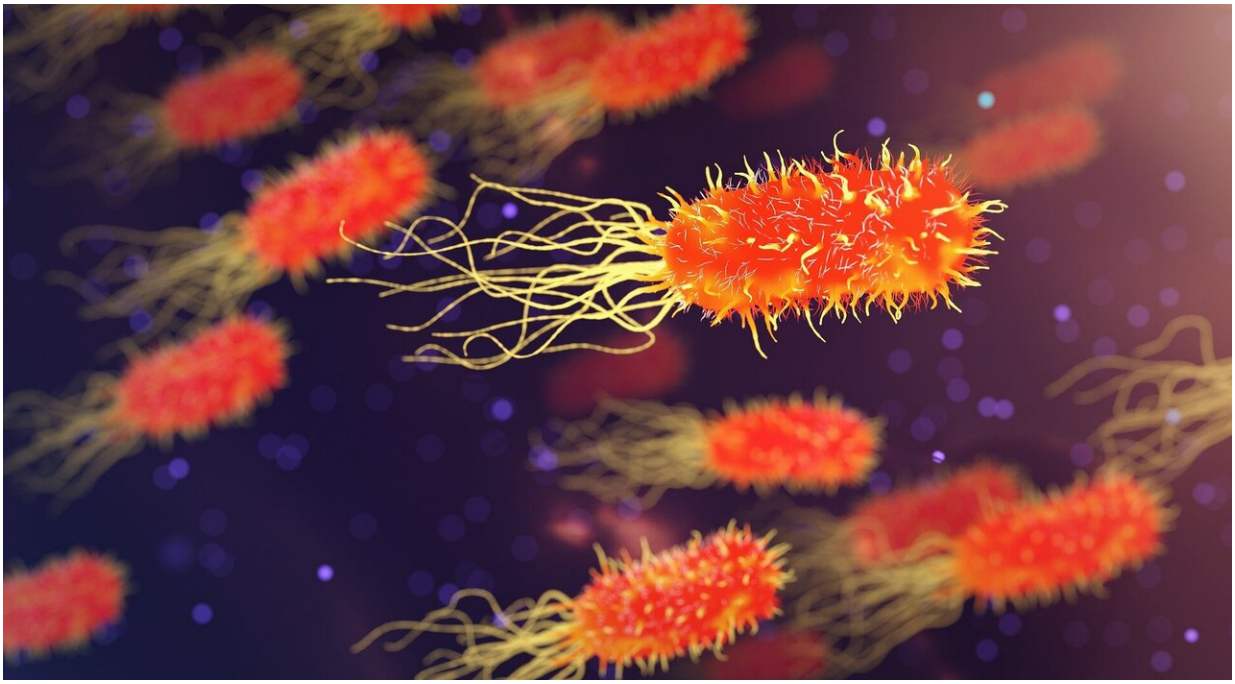

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A new study from researchers at San Diego State University suggests that ancient viruses called biophages may be just the set of garden tools needed to cultivate a healthy microbiome.

One need look no further than the nation's multi-billion-dollar probiotics industry to understand that many people are entranced by the notion of

influencing the complex community of bacteria and other microorganisms that live in the human gut.

In recent years, study after study has said that the overall health of this internal ecosystem is critical for overall health and can play a major factor in the development of diseases such as obesity, diabetes and cancer. But research has also shown that simply swallowing pills filled with beneficial bacteria often has no effect on the microbiome, which is made up of tens of trillions of microorganisms.

While the 1,000 or so species of bacteria in the gut tend to get all of the attention, there are also a massive number of biophage viruses swirling around in this complex mix.

A team of researchers led by molecular biologist Lance Boling and microbial ecologist Forest Rohwer found that foods such as artificial sweeteners, licorice, honey, hot sauce and oregano can stimulate or suppress this omnipresent force. In limited cases, the team found that some foods could be used to induce phages to kill harmful bacteria or encourage the growth of those that are beneficial.

This garden tool model for biophages is somewhat different than the role that has recently garnered them outsize attention.

With many bacteria now resistant to antibiotics, phages have recently been in the spotlight for their hunter killer abilities. San Diego is home to one of the highest-profile examples of phage power. When other treatments failed, a careful and experimental application of the tiny viruses killed the out-of-control infection that put UC San Diego comparative psychologist Thomas Patterson into a months-long coma.

In that case, Patterson's wife, UCSD infectious disease epidemiologist Steffanie Strathdee, and a wide-ranging team of clinicians and

researchers from academia and the U.S. Navy, searched for the right phages, selecting the very few from billions of possibilities that would attack the particular strain of toxin-producing acinetobacter baumannii bacteria that had left Patterson on the verge of death despite months of spare-no-expense intensive care.

Bacteriophages, at least those that attack and destroy bacteria anyway, are extremely specific. They'll gun for one bacteria species and leave every other bug alone.

But that's not the only way these simple viruses work. Some function as "prophages" living inside their preferred bacterial hosts and often contributing DNA segments that the bacteria can use to help themselves resist antibiotics or even process carbohydrates. Some substances, such as the antibiotic ciprofloxacin, induce prophages already living inside bacteria to leave suddenly, killing their hosts in the process.

It's a particularly-elegant solution, because there is no need to find the right phage to fight a specific bacteria as was the case for Patterson. The right virus to do the job is already inside the target and simply has to be induced to change its behavior from help to harm.

"What we call phage induction, it causes these viruses that are already present to activate and effectively blow up the bacteria," Rohwer said.

The SDSU team tested 117 different "consumable compounds" on four different bacteria and found that a handful of substances were particularly able to turn prophages rogue.

The compound stevia, a commonly used sugar substitute, showed a strong ability to induce prophages in a strain of Bacteroides thetaiotaomicron bacteria while the best results in another potentially-harmful microbe called enterococcus faecalis were uva ursi, propolis and

aspartame. The first is commonly called bearberry, the second is a resin collected by bees and the third an artificial sweetener. Tests also showed that stevia, grapefruit seed extract and toothpaste were the strongest prophage inducers for staphylococcus aureus, a third bacteria tested.

Other compounds such as rhubarb, fernet, coffee arabica and oregano reduced the number of viral particles across all types of bacteria tested. Some compounds, including hot sauces, were found to be broadly antimicrobial but did not have the exquisite level of specificity made possible by prophage induction. Tabasco hot sauce was the broadest bacteria burner of the bunch.

The sauce from Louisiana contains capsaicin and vinegar, both compounds known to have antibiotic properties. But there was definitely some Cajun mystery present in Tabasco.

"The Tabasco seemed to have something like a synergistic effect that was more powerful than what you might see just by combining vinegar and capsaicin," Boling said.

Though the antibacterial properties of some tested compounds, especially propolis and stevia, have already been observed, the study's results suggest that it is possible to selectively encourage and kill different bacteria in the human microbiome through the judicious use of foods with inhibitory and promotional properties.

Given that the health of the gut microbiome is shown to affect everything from cognitive ability and mood to weight and inflammation, the idea of purposefully tending this particular garden intrigues Steffanie Strathdee, the UCSD professor who helped save her husband's life with phages and now is co-director of UC San Diego's Center for Innovative Phage Applications and Theraputics.

"I think that, if you can show you can induce or inhibit phages reliably, then you can pursue this landscaping kind of approach where you can select what you want to grow and keep other things from growing," Strathdee said.

She noted that the findings in the SDSU paper, while promising, are not yet conclusive. The study, for example, tested only four bacteria among what are thought to be up to 1,000 different species present in the gut, meaning that broader testing will be necessary to understand whether findings with the four species tested are more broadly applicable. And, because the SDSU experiments were done under lab conditions, results might be different when tested inside the human body.

"It's a very complex system once you're testing inside the body, so we don't really know fully what the effects would be there," Strathdee said. "But it's pretty neat to think that maybe some day, dietary changes could be prescribed to improve health not just using phages to treat disease but also to promote health."

The study appears in the latest edition of the research journal *Gut Microbes.*